

10/574129

JAP5 Rec'd PCT/PTO 31 MAR 2006

SEQUENCE LISTING

| | | |
|----|---|------|
| | aaa gca cag atg aat tgc ttt tat ttg aaa gcc ttg gat ggt ttt gtt Lys Ala Gln Met Asn Cys Phe Tyr Leu Lys Ala Leu Asp Gly Phe Val 85 90 95 100 | 584 |
| 5 | atg gtt ctc aca gat gat ggt gac atg att tac att tct gat aat gtg Met Val Leu Thr Asp Asp Gly Asp Met Ile Tyr Ile Ser Asp Asn Val 105 110 115 | 632 |
| 10 | aac aaa tac atg gga tta act cag ttt gaa cta act gga cac agt gtg Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr Gly His Ser Val 120 125 130 | 680 |
| 15 | ttt gat ttt act cat cca tgt gac cat gag gaa atg aga gaa atg ctt Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met Arg Glu Met Leu 135 140 145 | 728 |
| 20 | aca cac aga aat ggc ctt gtg aaa aag ggt aaa gaa caa aac aca cag Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu Gln Asn Thr Gln 150 155 160 | 776 |
| 25 | cga agc ttt ttt ctc aga atg aag tgt acc cta act agc cga gga aga Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr Ser Arg Gly Arg 165 170 175 180 | 824 |
| 30 | act atg aac ata aag tct gca aca tgg aag gta ttg cac tgc aca ggc Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu His Cys Thr Gly 185 190 195 | 872 |
| 35 | cac att cac gta tat gat acc aac agt aac caa cct cag tgt ggg tat His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro Gln Cys Gly Tyr 200 205 210 | 920 |
| 40 | aag aaa cca cct atg acc tgc ttg gtg ctg att tgt gaa ccc att cct Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys Glu Pro Ile Pro 215 220 225 | 968 |
| 45 | cac cca tca aat att gaa att cct tta gat agc aag act ttc ctc agt His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys Thr Phe Leu Ser 230 235 240 | 1016 |
| 50 | cga cac agc ctg gat atg aaa ttt tct tat tgt gat gaa aga att acc Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp Glu Arg Ile Thr 245 250 255 260 | 1064 |
| 55 | gaa ttg atg gga tat gag cca gaa gaa ctt tta ggc cgc tca att tat Glu Leu Met Gly Tyr Glu Pro Glu Leu Leu Gly Arg Ser Ile Tyr 265 270 275 | 1112 |
| 60 | gaa tat tat cat gct ttg gac tct gat cat ctg acc aaa act cat cat Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr Lys Thr His His 280 285 290 | 1160 |
| | gat atg ttt act aaa gga caa gtc acc aca gga cag tac agg atg ctt Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln Tyr Arg Met Leu 295 300 305 | 1208 |
| | gcc aaa aga ggt gga tat gtc tgg gtt gaa act caa gca act gtc ata Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln Ala Thr Val Ile 310 315 320 | 1256 |
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| 5 | aca gaa tgt gtc ctt aaa ccg gtt gaa tct tca gat atg aaa atg act Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp Met Lys Met Thr 360 365 370 | 1400 |
| 10 | cag cta ttc acc aaa gtt gaa tca gaa gat aca agt agc ctc ttt gac Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser Ser Leu Phe Asp 375 380 385 | 1448 |
| 15 | aaa ctt aag aag gaa cct gat gct tta act ttg ctg gcc cca gcc gct Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu Ala Pro Ala Ala 390 395 400 | 1496 |
| 20 | gga gac aca atc ata tct tta gat ttt ggc agc aac gac aca gaa act Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn Asp Thr Glu Thr 405 410 415 420 | 1544 |
| 25 | gat gac cag caa ctt gag gaa gta cca tta tat aat gat gta atg ctc Asp Asp Gln Gln Leu Glu Val Pro Leu Tyr Asn Asp Val Met Leu 425 430 435 | 1592 |
| 30 | ccc tca ccc aac gaa aaa tta cag aat ata aat ttg gca atg tct cca Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu Ala Met Ser Pro 440 445 450 | 1640 |
| 35 | tta ccc acc gct gaa acg cca aag cca ctt cga agt agt gct gac cct Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser Ser Ala Asp Pro 455 460 465 | 1688 |
| 40 | gca ctc aat caa gaa gtt gca tta aaa tta gaa cca aat cca gag tca Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro Asn Pro Glu Ser 470 475 480 | 1736 |
| 45 | ctg gaa ctt tct ttt acc atg ccc cag att cag gat cag aca cct agt Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp Gln Thr Pro Ser 485 490 495 500 | 1784 |
| 50 | cct tcc gat gga agc act aga caa agt tca cct gag cct aat agt ccc Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu Pro Asn Ser Pro 505 510 515 | 1832 |
| 55 | agt gaa tat tgt ttt tat gtg gat agt gat atg gtc aat gaa ttc aag Ser Glu Tyr Cys Phe Tyr Val Asp Ser Asp Met Val Asn Glu Phe Lys 520 525 530 | 1880 |
| 60 | ttg gaa ttg gta gaa aaa ctt ttt gct gaa gac aca gaa gca aag aac Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr Glu Ala Lys Asn 535 540 545 | 1928 |
| 65 | cca ttt tct act cag gac aca gat tta gac ttg gag atg tta gct ccc Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu Met Leu Ala Pro 550 555 560 | 1976 |
| 70 | tat atc cca atg gat gat gac ttc cag tta cgt tcc ttc gat cag ttg Tyr Ile Pro Met Asp Asp Phe Gln Leu Arg Ser Phe Asp Gln Leu 565 570 575 580 | 2024 |
| 75 | tca cca tta gaa agc agt tcc gca agc cct gaa agc gca agt cct caa Ser Pro Leu Glu Ser Ser Ala Ser Pro Glu Ser Ala Ser Pro Gln 585 590 595 | 2072 |

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|----|--|------|
| | agc aca gtt aca gta ttc cag cag actcaa ata caa gaa cct act gct Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln Glu Pro Thr Ala | 2120 |
| | 600 605 610 | |
| 5 | aat gcc acc act acc act gcc acc act gat gaa tta aaa aca gtg aca Asn Ala Thr Thr Thr Ala Thr Thr Asp Glu Leu Lys Thr Val Thr | 2168 |
| | 615 620 625 | |
| 10 | aaa gac cgt atg gaa gac att aaa ata ttg att gca tct cca tct cct Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala Ser Pro Ser Pro | 2216 |
| | 630 635 640 | |
| 15 | acc cac ata cat aaa gaa act act agt gcc aca tca tca cca tat aga Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser Ser Pro Tyr Arg | 2264 |
| | 645 650 655 660 | |
| 20 | gat act caa agt cg ^g aca gcc tca cca aac aga gca gga aaa gga gtc Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala Gly Lys Gly Val | 2312 |
| | 665 670 675 | |
| | ata gaa cag aca gaa aaa tct cat cca aga agc cct aac gtg tta tct Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro Asn Val Leu Ser | 2360 |
| | 680 685 690 | |
| 25 | gtc gct ttg agt caa aga act aca gtt cct gag gaa gaa cta aat cca Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu Glu Leu Asn Pro | 2408 |
| | 695 700 705 | |
| 30 | aag ata cta gct ttg cag aat gct cag aga aag cga aaa atg gaa cat Lys Ile Leu Ala Leu Gln Asn Ala Gln Arg Lys Arg Lys Met Glu His | 2456 |
| | 710 715 720 | |
| 35 | gat ggt tca ctt ttt caa gca gta gga att gga aca tta tta cag cag Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr Leu Leu Gln Gln | 2504 |
| | 725 730 735 740 | |
| 40 | cca gac gat cat gca gct act aca tca ctt tct tgg aaa cgt gta aaa Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp Lys Arg Val Lys | 2552 |
| | 745 750 755 | |
| | gga tgc aaa tct agt gaa cag aat gga atg gag caa aag aca att att Gly Cys Lys Ser Ser Glu Gln Asn Gly Met Glu Gln Lys Thr Ile Ile | 2600 |
| | 760 765 770 | |
| 45 | tta ata ccc tct gat tta gca tgt aga ctg ctg ggg caa tca atg gat Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly Gln Ser Met Asp | 2648 |
| | 775 780 785 | |
| 50 | gaa agt gga tta cca cag ctg acc agt tat gat tgt gaa gtt aat gct Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys Glu Val Asn Ala | 2696 |
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| 55 | cct ata caa ggc agc aga aac cta ctg cag ggt gaa gaa tta ctc aga Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu Glu Leu Leu Arg | 2744 |
| | 805 810 815 820 | |
| 60 | gct ttg gat caa gtt aac tga gctttttctt aatttcatttc ctttttttgg Ala Leu Asp Gln Val Asn | 2795 |
| | 825 | |
| | acactggtgg ctcactacct aaaggagtct atttatattt tctacatcta atttttagaag | 2855 |
| | cctggctaca atactgcaca aacttggta gttcaatttt tgatcccattt tctacttaat | 2915 |

| | | |
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| | ttacattaat gctctttttt agtatgttct ttaatgctgg atcacagaca gtcatttc | 2975 |
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| 5 | tttattttttt tattttggc tagggagttt atccctttt cgaattttt ttaagaagat | 3095 |
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| 20 | gtggcattta tttggataaa attctcaatt cagagaaatc atctgatgtt tctatagtca | 3515 |
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| | tgtaactgat attaaaccta aatgttctgc ctaccctgtt ggtataaaga tattttgagc | 3635 |
| 25 | agactgtaaa caagaaaaaa aaaatcatgc attcttagca aaattgccta gtatgttaat | 3695 |
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| 30 | tgttagatttc aataattgag taattttaga agcattattt taggaatata tagttgtcac | 3815 |
| | agtaaatatc ttgtttttc tatgtacatt gtacaaattt ttcattcctt ttgctcttg | 3875 |
| | tggttggatc taacactaac tgtattgttt tgttacatca aataaacatc ttctgtggac | 3935 |
| 35 | caggaaaaaa aaaaaaaaaa aaa | 3958 |
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| | <211> 826 | |
| 40 | <212> PRT | |
| | <213> Homo sapiens | |
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| 45 | Met Glu Gly Ala Gly Gly Ala Asn Asp Lys Lys Lys Ile Ser Ser Glu | |
| | 1 5 10 15 | |
| | Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys | |
| 50 | 20 25 30 | |
| | Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His | |
| | 35 40 45 | |
| 55 | Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile | |
| | 50 55 60 | |
| 60 | Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Asp Leu Asp Ile | |
| | 65 70 75 80 | |

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|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | Glu | Asp | Asp | Met | Lys | Ala | Gln | Met | Asn | Cys | Phe | Tyr | Leu | Lys | Ala | Leu |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| 5 | Asp | Gly | Phe | Val | Met | Val | Leu | Thr | Asp | Asp | Gly | Asp | Met | Ile | Tyr | Ile |
| | | | | 100 | | | | 105 | | | | | 110 | | | |
| 10 | Ser | Asp | Asn | Val | Asn | Lys | Tyr | Met | Gly | Leu | Thr | Gln | Phe | Glu | Leu | Thr |
| | | | | 115 | | | | 120 | | | | | 125 | | | |
| 15 | Gly | His | Ser | Val | Phe | Asp | Phe | Thr | His | Pro | Cys | Asp | His | Glu | Glu | Met |
| | | | | 130 | | | | 135 | | | | | 140 | | | |
| 20 | Arg | Glu | Met | Leu | Thr | His | Arg | Asn | Gly | Leu | Val | Lys | Lys | Gly | Lys | Glu |
| | | | | 145 | | | | 150 | | | 155 | | | 160 | | |
| 25 | Gln | Asn | Thr | Gln | Arg | Ser | Phe | Phe | Leu | Arg | Met | Lys | Cys | Thr | Leu | Thr |
| | | | | 165 | | | | 170 | | | | | 175 | | | |
| 30 | Ser | Arg | Gly | Arg | Thr | Met | Asn | Ile | Lys | Ser | Ala | Thr | Trp | Lys | Val | Leu |
| | | | | 180 | | | | 185 | | | | | 190 | | | |
| 35 | His | Cys | Thr | Gly | His | Ile | His | Val | Tyr | Asp | Thr | Asn | Ser | Asn | Gln | Pro |
| | | | | 195 | | | | 200 | | | | | 205 | | | |
| 40 | Gln | Cys | Gly | Tyr | Lys | Lys | Pro | Pro | Met | Thr | Cys | Leu | Val | Leu | Ile | Cys |
| | | | | 210 | | | | 215 | | | | | 220 | | | |
| 45 | Glu | Pro | Ile | Pro | His | Pro | Ser | Asn | Ile | Glu | Ile | Pro | Leu | Asp | Ser | Lys |
| | | | | 225 | | | | 230 | | | 235 | | | 240 | | |
| 50 | Thr | Phe | Leu | Ser | Arg | His | Ser | Leu | Asp | Met | Lys | Phe | Ser | Tyr | Cys | Asp |
| | | | | 245 | | | | 250 | | | | | 255 | | | |
| 55 | Glu | Arg | Ile | Thr | Glu | Leu | Met | Gly | Tyr | Glu | Pro | Glu | Glu | Leu | Leu | Gly |
| | | | | 260 | | | | 265 | | | | | 270 | | | |
| 60 | Arg | Ser | Ile | Tyr | Glu | Tyr | Tyr | His | Ala | Leu | Asp | Ser | Asp | His | Leu | Thr |
| | | | | 275 | | | | 280 | | | | | 285 | | | |
| 65 | Lys | Thr | His | His | Asp | Met | Phe | Thr | Lys | Gly | Gln | Val | Thr | Thr | Gly | Gln |
| | | | | 290 | | | | 295 | | | | | 300 | | | |
| 70 | Tyr | Arg | Met | Leu | Ala | Lys | Arg | Gly | Gly | Tyr | Val | Trp | Val | Glu | Thr | Gln |
| | | | | 305 | | | | 310 | | | 315 | | | 320 | | |
| 75 | Ala | Thr | Val | Ile | Tyr | Asn | Thr | Lys | Asn | Ser | Gln | Pro | Gln | Cys | Ile | Val |
| | | | | 325 | | | | 330 | | | | | 335 | | | |

| | | | | | | | | | | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | Cys | Val | Asn | Tyr | Val | Val | Ser | Gly | Ile | Ile | Gln | His | Asp | Leu | Ile | Phe |
| | | | | | 340 | | | | 345 | | | | | 350 | | |
| 5 | Ser | Leu | Gln | Gln | Thr | Glu | Cys | Val | Leu | Lys | Pro | Val | Glu | Ser | Ser | Asp |
| | | | | | 355 | | | 360 | | | | 365 | | | | |
| 10 | Met | Lys | Met | Thr | Gln | Leu | Phe | Thr | Lys | Val | Glu | Ser | Glu | Asp | Thr | Ser |
| | | | | | 370 | | | 375 | | | | 380 | | | | |
| 15 | Ser | Leu | Phe | Asp | Lys | Leu | Lys | Lys | Glu | Pro | Asp | Ala | Leu | Thr | Leu | Leu |
| | | | | | 385 | | | 390 | | | 395 | | | 400 | | |
| 20 | Ala | Pro | Ala | Ala | Gly | Asp | Thr | Ile | Ile | Ser | Leu | Asp | Phe | Gly | Ser | Asn |
| | | | | | 405 | | | | 410 | | | | 415 | | | |
| 25 | Asp | Thr | Glu | Thr | Asp | Asp | Gln | Gln | Leu | Glu | Glu | Val | Pro | Leu | Tyr | Asn |
| | | | | | 420 | | | | 425 | | | | 430 | | | |
| 30 | Asp | Val | Met | Leu | Pro | Ser | Pro | Asn | Glu | Lys | Leu | Gln | Asn | Ile | Asn | Leu |
| | | | | | 435 | | | | 440 | | | | 445 | | | |
| 35 | Ala | Met | Ser | Pro | Leu | Pro | Thr | Ala | Glu | Thr | Pro | Lys | Pro | Leu | Arg | Ser |
| | | | | | 450 | | | | 455 | | | 460 | | | | |
| 40 | Ser | Ala | Asp | Pro | Ala | Leu | Asn | Gln | Glu | Val | Ala | Leu | Lys | Leu | Glu | Pro |
| | | | | | 465 | | | 470 | | | 475 | | | 480 | | |
| 45 | Asn | Pro | Glu | Ser | Leu | Glu | Leu | Ser | Phe | Thr | Met | Pro | Gln | Ile | Gln | Asp |
| | | | | | 485 | | | | 490 | | | | 495 | | | |
| 50 | Gln | Thr | Pro | Ser | Pro | Ser | Asp | Gly | Ser | Thr | Arg | Gln | Ser | Ser | Pro | Glu |
| | | | | | 500 | | | | 505 | | | | 510 | | | |
| 55 | Pro | Asn | Ser | Pro | Ser | Glu | Tyr | Cys | Phe | Tyr | Val | Asp | Ser | Asp | Met | Val |
| | | | | | 515 | | | | 520 | | | | 525 | | | |
| 60 | Asn | Glu | Phe | Lys | Leu | Glu | Leu | Val | Glu | Lys | Leu | Phe | Ala | Glu | Asp | Thr |
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| 70 | Met | Leu | Ala | Pro | Tyr | Ile | Pro | Met | Asp | Asp | Asp | Phe | Gln | Leu | Arg | Ser |
| | | | | | 565 | | | | 570 | | | | 575 | | | |
| 75 | Phe | Asp | Gln | Leu | Ser | Pro | Leu | Glu | Ser | Ser | Ser | Ala | Ser | Pro | Glu | Ser |
| | | | | | 580 | | | | 585 | | | | 590 | | | |

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|----|---|-----|-----|-----|
| | Ala Ser Pro Gln Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln | | | |
| | 595 | 600 | 605 | |
| 5 | Glu Pro Thr Ala Asn Ala Thr Thr Thr Thr Ala Thr Thr Asp Glu Leu | | | |
| | 610 | 615 | 620 | |
| 10 | Lys Thr Val Thr Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala | | | |
| | 625 | 630 | 635 | 640 |
| 15 | Ser Pro Ser Pro Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser | | | |
| | 645 | 650 | 655 | |
| 20 | Ser Pro Tyr Arg Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala | | | |
| | 660 | 665 | 670 | |
| 25 | Gly Lys Gly Val Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro | | | |
| | 675 | 680 | 685 | |
| 30 | Asn Val Leu Ser Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu | | | |
| | 690 | 695 | 700 | |
| 35 | Glu Leu Asn Pro Lys Ile Leu Ala Leu Gln Asn Ala Gln Arg Lys Arg | | | |
| | 705 | 710 | 715 | 720 |
| 40 | Lys Met Glu His Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr | | | |
| | 725 | 730 | 735 | |
| 45 | Leu Leu Gln Gln Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp | | | |
| | 740 | 745 | 750 | |
| 50 | Lys Arg Val Lys Gly Cys Lys Ser Ser Glu Gln Asn Gly Met Glu Gln | | | |
| | 755 | 760 | 765 | |
| 55 | Lys Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly | | | |
| | 770 | 775 | 780 | |
| 60 | Gln Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys | | | |
| | 785 | 790 | 795 | 800 |
| 55 | Glu Val Asn Ala Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu | | | |
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| 60 | Glu Leu Leu Arg Ala Leu Asp Gln Val Asn | | | |
| | 820 | 825 | | |
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| 20 | aag atg agt tct gaa cgt cga aaa gaa aag tct aga gat gca gca aga Lys Met Ser Ser Glu Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg 15 20 25 | 338 |
| 25 | tct cgg cga agc aaa gag tct gaa gtt ttt tat gag ctt gct cat cag Ser Arg Arg Ser Lys Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln 30 35 40 | 386 |
| 30 | ttg cca ctt ccc cac aat gtg agc tca cat ctt gat aaa gct tct gtt Leu Pro Leu Pro His Asn Val Ser Ser His Leu Asp Lys Ala Ser Val 45 50 55 | 434 |
| 35 | atg agg ctc acc atc agt tat tta cgt gtg aga aaa ctt ctg gat gcc Met Arg Leu Thr Ile Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala 60 65 70 75 | 482 |
| 40 | ggt ggt cta gac agt gaa gat gag atg aag gca cag atg gac tgt ttt Gly Gly Leu Asp Ser Glu Asp Glu Met Lys Ala Gln Met Asp Cys Phe 80 85 90 | 530 |
| 45 | tat ctg aaa gcc cta gat ggc ttt gtg atg gtg cta aca gat gac ggc Tyr Leu Lys Ala Leu Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly 95 100 105 | 578 |
| 50 | gac atg gtt tac att tct gat aac gtg aac aaa tac atg ggg tta act Asp Met Val Tyr Ile Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr 110 115 120 | 626 |
| 55 | cag ttt gaa cta act gga cac agt gtg ttt gat ttt act cat cca tgt Gln Phe Glu Leu Thr Gly His Ser Val Phe Asp Phe Thr His Pro Cys 125 130 135 | 674 |
| 60 | gac cat gag gaa atg aga gaa atg ctt aca cac aga aat ggc cca gtg Asp His Glu Glu Met Arg Glu Met Leu Thr His Arg Asn Gly Pro Val 140 145 150 155 | 722 |
| 65 | aga aaa ggg aaa gaa cta aac aca cag cgg agc ttt ttt ctc aga atg Arg Lys Gly Lys Glu Leu Asn Thr Gln Arg Ser Phe Phe Leu Arg Met 160 165 170 | 770 |
| 70 | aag tgc acc cta aca agc cgg ggg agg acg atg aac atc aag tca gca Lys Cys Thr Leu Thr Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala 175 180 185 | 818 |

| | | | | | |
|----|---|-----|-----|------|------|
| | acg tgg aag gtg ctt cac tgc acg ggc cat att cat gtc tat gat acc Thr Trp Lys Val Leu His Cys Thr Gly His Ile His Val Tyr Asp Thr 190 | 195 | 200 | 866 | |
| 5 | aac agt aac caa cct cag tgt ggg tac aag aaa cca ccc atg acg tgc Asn Ser Asn Gln Pro Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys 205 | 210 | 215 | 914 | |
| 10 | ttg gtg ctg att tgt gaa ccc att cct cat ccg tca aat att gaa att Leu Val Leu Ile Cys Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile 220 | 225 | 230 | 235 | 962 |
| 15 | cct tta gat agc aag aca ttt ctc agt cga cac agc ctc gat atg aaa Pro Leu Asp Ser Lys Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys 240 | 245 | 250 | 1010 | |
| 20 | ttt tct tac tgt gat gaa aga att act gag ttg atg ggt tat gag ccg Phe Ser Tyr Cys Asp Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro 255 | 260 | 265 | 1058 | |
| | gaa gaa ctt ttg ggc cgc tca att tat gaa tat tat cat gct ttg gat Glu Glu Leu Leu Gly Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp 270 | 275 | 280 | 1106 | |
| 25 | tct gat cat ctg acc aaa act cac cat gat atg ttt act aaa gga caa Ser Asp His Leu Thr Lys Thr His His Asp Met Phe Thr Lys Gly Gln 285 | 290 | 295 | 1154 | |
| 30 | gtc acc aca gga cag tac agg atg ctt gcc aaa aga ggt gga tat gtc Val Thr Thr Gly Gln Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val 300 | 305 | 310 | 315 | 1202 |
| 35 | tgg gtt gaa act caa gca act gtc ata tat aat acg aag aac tcc cag Trp Val Glu Thr Gln Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln 320 | 325 | 330 | 1250 | |
| 40 | cca cag tgc att gtg tgt gtg aat tat gtt gta agt ggt att att cag Pro Gln Cys Ile Val Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln 335 | 340 | 345 | 1298 | |
| | cac gac ttg att ttc tcc ctt caa caa aca gaa tct gtg ctc aaa cca His Asp Leu Ile Phe Ser Leu Gln Gln Thr Glu Ser Val Leu Lys Pro 350 | 355 | 360 | 1346 | |
| 45 | gtt gaa tct tca gat atg aag atg act cag ctg ttc acc aaa gtt gaa Val Glu Ser Ser Asp Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu 365 | 370 | 375 | 1394 | |
| 50 | tca gag gat aca agc tgc ctt ttt gat aag ctt aag aag gag cct gat Ser Glu Asp Thr Ser Cys Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp 380 | 385 | 390 | 395 | 1442 |
| 55 | gct ctc act ctg ctg gct cca gct gcc ggc gac acc atc atc tct ctg Ala Leu Thr Leu Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu 400 | 405 | 410 | 1490 | |
| 60 | gat ttt ggc agc gat gac aca gaa act gaa gat caa caa ctt gaa gat Asp Phe Gly Ser Asp Asp Thr Glu Thr Glu Asp Gln Gln Leu Glu Asp 415 | 420 | 425 | 1538 | |
| | gtt cca tta tat aat gat gta atg ttt ccc tct tct aat gaa aaa tta Val Pro Leu Tyr Asn Asp Val Met Phe Pro Ser Ser Asn Glu Lys Leu 430 | 435 | 440 | 1586 | |

| | | |
|----|---|------|
| | aat ata aac ctg gca atg tct cct tta cct tca tcg gaa act cca aag Asn Ile Asn Leu Ala Met Ser Pro Leu Pro Ser Ser Glu Thr Pro Lys 445 450 455 | 1634 |
| 5 | cca ctt cga agt agt gct gat cct gca ctg aat caa gag gtt gca tta Pro Leu Arg Ser Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu 460 465 470 475 | 1682 |
| 10 | aaa tta gaa tca agt cca gag tca ctg gga ctt tct ttt acc atg ccc Lys Leu Glu Ser Ser Pro Glu Ser Leu Gly Leu Ser Phe Thr Met Pro 480 485 490 | 1730 |
| 15 | cag att caa gat cag cca gca agt cct tct gat gga agc act aga caa Gln Ile Gln Asp Gln Pro Ala Ser Pro Ser Asp Gly Ser Thr Arg Gln 495 500 505 | 1778 |
| 20 | agt tca cct gag aga ctt ctt cag gaa aac gta aac act cct aac ttt Ser Ser Pro Glu Arg Leu Leu Gln Glu Asn Val Asn Thr Pro Asn Phe 510 515 520 | 1826 |
| 25 | tcc cag cct aac agt ccc agt gaa tat tgc ttt gat gtg gat agc gat Ser Gln Pro Asn Ser Pro Ser Glu Tyr Cys Phe Asp Val Asp Ser Asp 525 530 535 | 1874 |
| 30 | atg gtc aat gta ttc aag ttg gaa ctg gtg gaa aaa ctg ttt gct gaa Met Val Asn Val Phe Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu 540 545 550 555 | 1922 |
| 35 | gac aca gag gca aag aat cca ttt tca act cag gac act gat tta gat Asp Thr Glu Ala Lys Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp 560 565 570 | 1970 |
| 40 | ttg gag atg ctg gct ccc tat atc cca atg gat gat gat ttc cag tta Leu Glu Met Leu Ala Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu 575 580 585 | 2018 |
| 45 | cgt tcc ttt gat cag ttg tca cca tta gag agc aat tct cca agc cct Arg Ser Phe Asp Gln Leu Ser Pro Leu Glu Ser Asn Ser Pro Ser Pro 590 595 600 | 2066 |
| 50 | cca agt atg agc aca gtt act ggg ttc cag cag acc cag tta cag aaa Pro Ser Met Ser Thr Val Thr Gly Phe Gln Gln Thr Gln Leu Gln Lys 605 610 615 | 2114 |
| 55 | cct acc atc act gcc act gcc acc aca act gcc acc act gat gaa tca Pro Thr Ile Thr Ala Thr Ala Thr Thr Ala Thr Thr Asp Glu Ser 620 625 630 635 | 2162 |
| 60 | aaa aca gag acg aag gac aat aaa gaa gat att aaa ata ctg att gca Lys Thr Glu Thr Lys Asp Asn Lys Glu Asp Ile Lys Ile Leu Ile Ala 640 645 650 | 2210 |
| | tct cca tct tct acc caa gta cct caa gaa acg acc act gct aag gca Ser Pro Ser Ser Thr Gln Val Pro Gln Glu Thr Thr Ala Lys Ala 655 660 665 | 2258 |
| | tca gca tac agt ggc act cac agt cgg aca gcc tca cca gac aga gca Ser Ala Tyr Ser Gly Thr His Ser Arg Thr Ala Ser Pro Asp Arg Ala 670 675 680 | 2306 |
| | gga aag aga gtc ata gaa cag aca gac aaa gct cat cca agg agc ctt Gly Lys Arg Val Ile Glu Gln Thr Asp Lys Ala His Pro Arg Ser Leu 685 690 695 | 2354 |

| | | |
|----|--|-------------------------------|
| | aag ctg tct gcc act ttg aat caa aga aat act gtt cct gag gaa gaa Lys Leu Ser Ala Thr Leu Asn Gln Arg Asn Thr Val Pro Glu Glu Glu 700 705 710 715 | 2402 |
| 5 | tta aac cca aag aca ata gct tcg cag aat gct cag agg aag cga aaa Leu Asn Pro Lys Thr Ile Ala Ser Gln Asn Ala Gln Arg Lys Arg Lys 720 725 730 | 2450 |
| 10 | atg gaa cat gat ggc tcc ctt ttt caa gca gca gga att gga aca tta Met Glu His Asp Gly Ser Leu Phe Gln Ala Ala Gly Ile Gly Thr Leu 735 740 745 | 2498 |
| 15 | ttg cag caa cca ggt gac tgt gca cct act atg tca ctt tcc tgg aaa Leu Gln Gln Pro Gly Asp Cys Ala Pro Thr Met Ser Leu Ser Trp Lys 750 755 760 | 2546 |
| 20 | cga gtg aaa gga ttc ata tct agt gaa cag aat gga acg gag caa aag Arg Val Lys Gly Phe Ile Ser Ser Glu Gln Asn Gly Thr Glu Gln Lys 765 770 775 | 2594 |
| 25 | act att att tta ata ccc tcc gat tta gca tgc aga ctg ctg ggg cag Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly Gln 780 785 790 795 | 2642 |
| 30 | tca atg gat gag agt gga tta cca cag ctg acc agt tac gat tgt gaa Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys Glu 800 805 810 | 2690 |
| 35 | gtt aat gct ccc ata caa ggc agc aga aac cta ctg cag ggt gaa gaa Val Asn Ala Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu Glu 815 820 825 | 2738 |
| 40 | tta ctc aga gct ttg gat caa gtt aac tga gcgtttccta atctcattcc Leu Leu Arg Ala Leu Asp Gln Val Asn 830 835 | 2788 |
| 45 | ttttgattgt taatgtttt gttcagttgt tgggtttgt tgggttttg tttctgttgg ttatttttgg acactggtgg ctcagcagtc tatttatatt ttctatatct aattttagaa gcctggctac aatactgcac aaactcagat agtttagtt tcatacccctt tctacttaat tttcattaat gctctttta atatgttctt ttaatgccag atcacagcac attcacagct cctcagcatt tcaccattgc attgctgttag tgtcatttaa aatgcacccctt tttatttatt tattttttgtt gagggagttt gtccttattt gaattatttt taatgaaatg ccaatataat | 2848 2908 2968 3028 3088 3148 |
| 50 | tttttaagaa agcagtaaat tctcatcatg atcataggca gttaaaaact ttttactcat tttttcatg ttttacatga aaataatgct ttgtcagcag tacatggtag ccacaattgc acaatatatt ttctttaaaa aaccagcagt tactcatgca atatattctg catttataaa actagttttt aagaaatttt ttttggccta tggaattgtt aagcctggat catgaagcgt tgatcttata atgattctta aactgtatgg tttcttata tggtaaagc catttacatg | 3208 3268 3328 3388 3448 |
| 55 | atataaaagaa atatgcttat atctggaagg tatgtggcat ttatggat aaaattctca attcagagaa gttatctggt gtttcttgac ttacccaact caaaacagtc cctctgttagt | 3508 3568 |
| 60 | tgtgaaagct tatgctaata ttgtgtaatt gattatgaaa cataaatggtt ctgcccaccc | 3628 |

| | | |
|----|--|------|
| | tgttggata aagacattt gagcatactg taaacaaaca aacaaaaaat catgcttgt | 3688 |
| 5 | tagtaaaatt gccttagtatg ttgattgtt gaaaatatga tgtttggtt tatgcactt | 3748 |
| | gtcgctatta acatcctttt ttcatataga tttcaataag tgagtaattt tagaaggatt | 3808 |
| | attttaggaa tatagagttg tcatalogtaaa catctgttt tttctatgtc cactgtataa | 3868 |
| 10 | attttcgtt cccttgctct ttgtgggtgg gtctaacact aactgtactg tttgttata | 3928 |
| | tcaaataaac atcttctgtg gaccaggaaa aaaaaaaaaa aaaaa | 3973 |
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| | 1 5 10 15 | |
| 25 | Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys | |
| | 20 25 30 | |
| 30 | Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His | |
| | 35 40 45 | |
| 35 | Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile | |
| | 50 55 60 | |
| 40 | Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Gly Leu Asp Ser | |
| | 65 70 75 80 | |
| 45 | Glu Asp Glu Met Lys Ala Gln Met Asp Cys Phe Tyr Leu Lys Ala Leu | |
| | 85 90 95 | |
| 50 | Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly Asp Met Val Tyr Ile | |
| | 100 105 110 | |
| 55 | Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr | |
| | 115 120 125 | |
| 60 | Gly His Ser Val Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met | |
| | 130 135 140 | |
| | Arg Glu Met Leu Thr His Arg Asn Gly Pro Val Arg Lys Gly Lys Glu | |
| | 145 150 155 160 | |
| | Leu Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr | |
| | 165 170 175 | |

Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu
 180 185 190

5 His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro
 195 200 205

10 Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys
 210 215 220

15 Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys
 225 230 235 240

20 Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp
 245 250 255

25 Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly
 260 265 270

30 Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr
 275 280 285

35 Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln
 290 295 300

40 Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln
 305 310 315 320

45 Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val
 325 330 335

50 Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe
 340 345 350

55 Ser Leu Gln Gln Thr Glu Ser Val Leu Lys Pro Val Glu Ser Ser Asp
 355 360 365

60 Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser
 370 375 380

55 Cys Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu
 385 390 395 400

60 Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asp
 405 410 415

Asp Thr Glu Thr Glu Asp Gln Gln Leu Glu Asp Val Pro Leu Tyr Asn
 420 425 430

| | | |
|----|---|-----|
| | Asp Val Met Phe Pro Ser Ser Asn Glu Lys Leu Asn Ile Asn Leu Ala | |
| | 435 | 440 |
| 5 | Met Ser Pro Leu Pro Ser Ser Glu Thr Pro Lys Pro Leu Arg Ser Ser | |
| | 450 | 455 |
| | 460 | |
| 10 | Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Ser Ser | |
| | 465 | 470 |
| | 475 | 480 |
| 15 | Pro Glu Ser Leu Gly Leu Ser Phe Thr Met Pro Gln Ile Gln Asp Gln | |
| | 485 | 490 |
| | 495 | |
| 20 | Pro Ala Ser Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu Arg | |
| | 500 | 505 |
| | 510 | |
| 25 | Leu Leu Gln Glu Asn Val Asn Thr Pro Asn Phe Ser Gln Pro Asn Ser | |
| | 515 | 520 |
| | 525 | |
| 30 | Pro Ser Glu Tyr Cys Phe Asp Val Asp Ser Asp Met Val Asn Val Phe | |
| | 530 | 535 |
| | 540 | |
| 35 | Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr Glu Ala Lys | |
| | 545 | 550 |
| | 555 | 560 |
| 40 | Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu Met Leu Ala | |
| | 565 | 570 |
| | 575 | |
| 45 | Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu Arg Ser Phe Asp Gln | |
| | 580 | 585 |
| | 590 | |
| 50 | Leu Ser Pro Leu Glu Ser Asn Ser Pro Ser Pro Pro Ser Met Ser Thr | |
| | 595 | 600 |
| | 605 | |
| 55 | Val Thr Gly Phe Gln Gln Thr Gln Leu Gln Lys Pro Thr Ile Thr Ala | |
| | 610 | 615 |
| | 620 | |
| 60 | Thr Ala Thr Thr Ala Thr Thr Asp Glu Ser Lys Thr Glu Thr Lys | |
| | 625 | 630 |
| | 635 | 640 |
| 55 | Asp Asn Lys Glu Asp Ile Lys Ile Leu Ile Ala Ser Pro Ser Ser Thr | |
| | 645 | 650 |
| | 655 | |
| 60 | Gln Val Pro Gln Glu Thr Thr Ala Lys Ala Ser Ala Tyr Ser Gly | |
| | 660 | 665 |
| | 670 | |
| | Thr His Ser Arg Thr Ala Ser Pro Asp Arg Ala Gly Lys Arg Val Ile | |
| | 675 | 680 |
| | 685 | |

Glu Gln Thr Asp Lys Ala His Pro Arg Ser Leu Lys Leu Ser Ala Thr
 690 695 700
 5
 Leu Asn Gln Arg Asn Thr Val Pro Glu Glu Glu Leu Asn Pro Lys Thr
 705 710 715 720
 10 Ile Ala Ser Gln Asn Ala Gln Arg Lys Arg Lys Met Glu His Asp Gly
 725 730 735
 15 Ser Leu Phe Gln Ala Ala Gly Ile Gly Thr Leu Leu Gln Gln Pro Gly
 740 745 750
 20 Asp Cys Ala Pro Thr Met Ser Leu Ser Trp Lys Arg Val Lys Gly Phe
 755 760 765
 Ile Ser Ser Glu Gln Asn Gly Thr Glu Gln Lys Thr Ile Ile Leu Ile
 770 775 780
 25 Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly Gln Ser Met Asp Glu Ser
 785 790 795 800
 30 Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys Glu Val Asn Ala Pro Ile
 805 810 815
 35 Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu Glu Leu Leu Arg Ala Leu
 820 825 830
 40 Asp Gln Val Asn
 835
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 <213> Artificial
 50 <220>
 <223> Generic sequence of an siRNA used to target human HIF-1α
 55 <220>
 <221> misc_feature
 <222> (20)..(28)
 <223> n can be any nucleotide, up to 4 of which can be missing,
 representing a single stranded loop of from 5-9 bases, the
 hairpin loop remaining single-stranded when bases 1-19 and 29-47
 hybridize to each other to form a duplex
 60 <220>
 <221> misc_feature
 <222> (48)..(55)
 <223> n can be any nucleotide, up to 6 of which can be missing,
 representing a 3' overhang of from 2-8 nucleotides, the 3'
 overhang remaining single stranded when the duplex forms between

nucleotides 1-19 and 29-47

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5      gatgacatga aagcacagan nnnnnnnntc tgtgcttca tgtcatcnnn nnnnn      55
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10     <211> 53
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15     <220>
15     <223> Specific sequence of an siRNA used to target human HIF-1a

20     <220>
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20     <222> (1)..(19)
20     <223> Sense strand of an siRNA used to target human HIF-1a. Sequence
20             corresponds to bases 528-546 of Genbank Accession No. NM_001530.
20             This sequence forms the double stranded region of a hairpin by
20             intramolecular hybridization with bases 29-47.

25     <220>
25     <221> misc_feature
25     <222> (20)..(28)
25     <223> 9 base loop structure, which stays single stranded when bases
25             1-19 and 29-47 form a duplex

30     <220>
30     <221> misc_feature
30     <222> (29)..(47)
30     <223> Antisense strand of an siRNA used to target human HIF-1a.
30             Sequence corresponds to the reverse complement of bases 528-546
30             of NM_001530. This sequence forms the double stranded region of
30             a hairpin by intramolecular hybridization with bases 1-19.

35     <220>
35     <221> misc_feature
35     <222> (48)..(53)
35     <223> 6 base 3' overhang, which stays single stranded when bases 1-19
35             and 29-47 form a duplex

40     <400> 6
40     gatgacatga aagcacagat tcaagagatc tgtgcttca tgtcatcttt ttt      53

45     <210> 7
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50     <400> 7
50     atgacatgaa agcacagat      19

55     <210> 8
55     <211> 21
55     <212> DNA
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60     <220>
60     <223> Artificial sense strand designed with no known homology to any
60             human gene to be used to create a negative control siRNA

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5  
  
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